continued safety, purity, potency, and effectiveness of the final product will not be adversely affected.

[42 FR 27583, May 31, 1977, as amended at 64 FR 26286, May 14, 1999]

§ 640.91 Processing.

(a) *Date of manufacture.* The date of manufacture shall be the date of final sterile filtration of a uniform pool of bulk solution.

(b) *Processing method.* The processing method shall not affect the integrity of the product, and shall have been shown to yield consistently a product which:

(1) After the heating prescribed in paragraph (e) of this section does not show an increase in the components with electrophoretic mobility similar to that of alpha globulin that amounts to more than 5 percent of the total protein.

(2) Contains less than 5 percent protein with a sedimentation coefficient greater than 7.0 S.

(3) Is safe for intravenous injection.

(c) *Microbial contamination.* All processing steps shall be conducted in a manner to minimize the risk of contamination from microorganisms, pyrogens, or other impurities. Preservatives to inhibit growth of microorganisms shall not be used during processing.

(d) *Storage of bulk fraction.* Bulk concentrate to be held more than 1 week prior to further processing shall be stored in clearly identified closed vessels at a temperature of −5 °C or colder. Any other bulk form of the product (exclusive of the sterile bulk solution) to be held more than 1 week prior to further processing, shall be stored in clearly identified closed vessels at a temperature of 5 °C or colder. Any bulk fraction to be held one week or less prior to further processing shall be stored in clearly identified closed vessels at a temperature of 5 °C or colder.

(e) *Heat treatment.* Heating of the final containers of Plasma Protein Fraction (Human) shall begin within 24 hours after completion of filling. Heat treatment shall be conducted so that the solution is heated continuously for not less than 10 or more than 11 hours at an attained temperature of 60±0.5 °C.

(f) *Stabilizer.* Either 0.08±0.016 millimole sodium caprylate, or 0.08±0.016 millimole sodium acetyltryptophanate and 0.08±0.016 millimole sodium caprylate per gram of protein shall be present as a stabilizer(s). Calculations of the stabilizer concentration may employ the labeled value 5 percent for the protein concentration of the product.

(g) *Incubation.* All final containers of Plasma Protein Fraction (Human) shall be incubated at 20 to 35 °C for at least 14 days following the heat treatment prescribed in paragraph (e) of this section. At the end of this incubation period, each final container shall be examined and all containers showing any indication of turbidity or microbial contamination shall not be issued. The contents of turbid final containers shall be examined microscopically and tested for sterility. If growth occurs, the types of organisms shall be identified as to genus and the material from such containers shall not be used for further manufacturing.

[42 FR 27583, May 31, 1977, as amended at 64 FR 26286, May 14, 1999]

§ 640.92 Tests on final product.

Tests shall be performed on the final product to determine that it meets the following standards:

(a) *Protein concentration.* The final product shall be a 5.0 ±0.30 percent solution of protein.

(b) *Protein composition.* The total protein in the final product shall consist of at least 83 percent albumin, and no more than 17 percent globulins. No more than 1 percent of the total protein shall be gamma globulin. The protein composition shall be determined by a method that has been approved for each manufacturer by the Director, Center for Biologics Evaluation and Research, Food and Drug Administration.

(c) *pH.* The pH shall be 7.0 ±0.3 when measured in a solution of the final product diluted to a concentration of 1 percent protein with 0.15 molar sodium chloride.

(d) *Sodium concentration.* The sodium concentration of the final product shall be 130 to 160 milliequivalents per liter.

(e) *Potassium concentration.* The potassium concentration of the final product shall not exceed 2 milliequivalents per liter.